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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	10/783,986
	Filing Date	February 19, 2004
	First Named Inventor	Ronit Satchi-Fainaro
	Art Unit	1614
	Examiner Name	To be assigned
Total Number of Pages in This Submission	Attorney Docket Number	701039-52584-CIP

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to Technology Center (TC)
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
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<input type="checkbox"/> Response to Missing Parts/Incomplete Application	The Commissioner is hereby authorized to charge any fee deficiency or credit any overpayment to the Nixon Peabody LLP Deposit Account No. 50-0850.	
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT	
Firm or Individual name	David S. Resnick (34,235) Nixon Peabody LLP, 100 Summer Street, Boston, MA 02110
Signature	
Date	July 12, 2004

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Signature		Date	July 13, 2004

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Practitioner's Docket No. 701039-052584-CIP

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Ronit Satchi-Fainaro; Judah M. Folkman
Application No.: 10/783,986 (CIP of PCT/US03/10976) Group No.: 1614
Filed: February 19, 2004 Examiner: To be assigned
For: TNP-470 SPECIES, POLYMER CONJUGATES AND USE THEREOF

MAIL STOP AMENDMENT
Commissioner for Patents
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Date: July 13, 2004

Linda M. Ginsberg

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with the provisions of 37 C.F.R. §§1.56 and 1.97, Applicants herewith submit the publications and/or patents shown on the attached form PTO-1449, for consideration by the Examiner in connection with the examination of the above-identified patent application.

I. REMARKS

In accordance with the provisions of 37 C.F.R. §1.97, this statement is being filed:

- X (1) within three (3) months of the Filing Date or before the mailing date of the First Office Action on the merits; or
- (2) within three months of the mailing date of the PCT International Search Report; or

- (3) after the period defined in (1) but before the mailing date of a **Final Rejection** or **Notice of Allowance**, and the requisite Certification or fee under Rule 1.17(p), namely **\$180.00**, is included herein; or
- (4) after the mailing date of a **Final Rejection** or **Notice of Allowance** but before the payment of the **Issue Fee**, and the requisite Certification, petition, and petition fee are included herein.

It is respectfully requested that each of the documents shown on the attached form(s) PTO-1449 be made of record in this application. Copies of these documents (CHECK ONE):

 X are enclosed herewith; and

— have been cited in the parent application, and are thus not being resubmitted herein.

Early examination and allowance of the present application are respectfully solicited.

FEE AUTHORIZATION

Should any fees associated with the submission be required, the Commissioner is authorized to charge the missing fee to our Deposit Account No. 50-0850. Any overpayments should be credited to said Deposit Account.

Respectfully submitted,



David S. Resnick (Reg. 34,235)
NIXON PEABODY LLP
100 Summer Street
Boston, MA 02110
(617) 345-6057

Date: July 12, 2004



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Substitute for form 1449 PTO

(use as many sheets as necessary)

Sheet	1	of	6
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Complete if Known

Application Number	10/783,986
Filing Date	February 19, 2004
First Named Inventor	Ronit Satchi-Fainaro et al.
Art Unit	1614
Examiner Name	To be assigned
Attorney Docket Number	701039-52584-CIP

U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

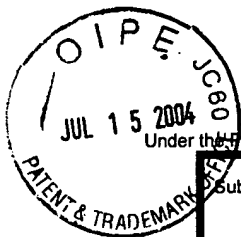
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Complete if Known			
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		First Named Inventor	Ronit Satchi-Fainaro et al.		
		Art Unit	1614		
		Examiner Name	To be assigned		
Sheet	2	of	6	Attorney Docket Number	701039-52584-CIP

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
	C1	Folkman, J., Angiogenesis. in <i>Harrison's Textbook of Internal Medicine</i> (eds. Braunwald, E. et al.) 517-530 (McGraw Hill, New York, 2001).	
	C2	Hanahan, D. et al., Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis, <i>Cell</i> , 86:353-64 (1996).	
	C3	Volpert, O.V. et al., Id1 regulates angiogenesis through transcriptional repression of thrombospondin-1, <i>Cancer Cell</i> , 2:473-483 (2002).	
	C4	Folkman, J., Tumor angiogenesis, <i>Cancer Medicine</i> (eds. Holland, J. et al.), pp. 132-152 (B. C. Decker Inc., Ontario, Canada, 2000).	
	C5	Lyden, D. et al., Id1 and Id3 are required for neurogenesis, angiogenesis and vascularization of tumour xenografts, <i>Nature</i> , 401:670-677 (1999).	
	C6	Streit, M. et al., Thrombospondin-2: a potent endogenous inhibitor of tumor growth and angiogenesis, <i>Proc Natl. Acad. Sci. USA</i> , 96:14888-14893 (1999).	
	C7	Chin, L. et al., Essential role for oncogenic Ras in tumour maintenance, <i>Nature</i> , 400:468-472 (1999).	
	C8	Tabone, M.D. et al., Are basic fibroblast growth factor and vascular endothelial growth factor prognostic indicators in pediatric patients with malignant solid tumors?, <i>Clinical Cancer Res.</i> , 7:538-543 (2001).	
	C9	Yao, Y. et al., Prognostic value of vascular endothelial growth factor and its receptors Flt-1 and Flk-1 in astrocytic tumours, <i>Acta Neurochir (Wien)</i> , 143:159-66 (2001).	
	C10	Yuan, A. et al., Aberrant p53 expression correlates with expression of vascular endothelial growth factor mRNA and interleukin-8 mRNA and neoangiogenesis in non-small-cell lung cancer, <i>J. Clinical Oncology</i> , 20:900-910 (2002).	

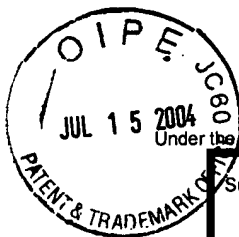
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Sheet	3	of	6	Attorney Docket Number	701039-52584-CIP

C11	Ingber, D. et al., Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumour growth, <i>Nature</i> , 348 :555-557 (1990).	
C12	Antoine, N. et al., AGM-1470, a potent angiogenesis inhibitor, prevents the entry of normal but not transformed endothelial cells into the G ₁ phase of the cell cycle, <i>Cancer Res.</i> , 54 :2073-2076 (1994).	
C13	Kudelka, A.P. et al., Complete remission of metastatic cervical cancer with the angiogenesis inhibitor TNP-470, <i>N. Engl. J. Med.</i> , 338 :991-2 (1998).	
C14	Kudelka, A.P. et al., A phase I study of TNP-470 administered to patients with advanced squamous cell cancer of the cervix, <i>Clinical Cancer Res.</i> , 3 :1501-1505 (1997).	
C15	Bhargava, P. et al., A Phase I and pharmacokinetic study of TNP-470 administered weekly to patients with advanced cancer, <i>Clinical Cancer Res.</i> , 5 :1989-1995 (1999).	
C16	Herbst, R.S. et al., Safety and pharmacokinetic effects of TNP-470, an angiogenesis inhibitor, combined with paclitaxel in patients with solid tumors: evidence for activity in non-small-cell lung cancer, <i>J. Clinical Oncol.</i> , 20 :4440-4447 (2002).	
C17	Kim, E.S. et al., Angiogenesis inhibitors in lung cancer. <i>Curr. Oncol. Rep.</i> , 4 :325-333 (2002).	
C18	Stadler, W.M. et al., Multi-institutional study of the angiogenesis inhibitor TNP-470 in metastatic renal carcinoma, <i>J. Clinical Oncol.</i> , 17 :2541-2545 (1999).	
C19	Logothetis, C.J. et al., Phase I trial of the angiogenesis inhibitor TNP-470 for progressive androgen-independent prostate cancer. <i>Clinical Cancer Res.</i> , 7 :1198-1203 (2001).	
C20	Rupnick, M.A. et al., Adipose tissue mass can be regulated through the vasculature, <i>Proc. Natl. Acad. Sci. U S A</i> , 99 :10730-10735 (2002).	
C21	Schoof, D.D. et al., The influence of angiogenesis inhibitor AGM-1470 on immune system status and tumor growth in vitro, <i>Int. J. Cancer</i> , 55 :630-635 (1993).	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Application Number	10/783,986	
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Sheet	4	of	6	Attorney Docket Number	701039-52584-CIP

	C22	Nagabuchi, E. et al., TNP-470 antiangiogenic therapy for advanced murine neuroblastoma, <i>J. Pediatric Surg.</i> , 32 :287-93 (1997).	
	C23	Rihova, B. et al., Biocompatibility of N-(2-hydroxypropyl) methacrylamide copolymers containing adriamycin. Immunogenicity, and effect on haematopoietic stem cells in bone marrow in vivo and mouse splenocytes and human peripheral blood lymphocytes in vitro, <i>Biomaterials</i> , 10 :335-342. (1989).	
	C24	Seymour, L.W. et al., The pharmacokinetics of polymer-bound adriamycin, <i>Biochem. Pharmacol.</i> , 39 :1125-1131 (1990).	
	C25	Maeda, H. et al., Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review, <i>J. Controlled Release</i> , 65 :271-284 (2000).	
	C26	Duncan, R. et al., Preclinical toxicology of a novel polymeric antitumour agent: HPMACopolymer-doxorubicin (PK1), <i>Human and Exp. Toxicology</i> , 17 :93-104 (1998).	
	C27	Satchi-Fainaro, R., Targeting tumor vasculature: Reality or a dream?. <i>J. Drug Targeting</i> , 10 :529-533 (2002).	
	C28	Duncan, R. et al., Polymers containing enzymatically degradable bonds, 7. Design of oligopeptide side chains in poly [N-(2-hydroxypropyl)methacrylamide] copolymers to promote efficient degradation by lysosomal enzymes, <i>Makromol. Chem.</i> , 184 :1997-2008 (1983).	
	C29	Foekens, J.A. et al., Prognostic significance of cathepsins B and L in primary human breast cancer. <i>J. Clinical Oncol.</i> , 16 :1013-1021 (1998).	
	C30	Gianasi, E. et al., HPMACopolymer platinates as novel antitumour agents: in vitro properties, pharmacokinetics and antitumour activity in vivo, <i>Eur. J. Cancer</i> , 35 :994-1002 (1999).	
	C31	Kusaka, M. et al. Cytostatic inhibition of endothelial cell growth by the angiogenesis inhibitor TNP-470 (AGM-1470), <i>Br. J. Cancer</i> . 69 :212-216 (1994).	
	C32	Greene, A.K. et al., Endothelial-directed hepatic regeneration after partial hepatectomy, <i>Ann. Surg.</i> , 237 :530-535 (2003)	

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Sheet	5	of	6	Attorney Docket Number	701039-52584-CIP

	C33	Drixler, T.A. et al., Liver regeneration is an angiogenesis- associated phenomenon, <i>Ann. Surg.</i> , 236 :703-712 (2002).	
	C34	Klein, S.A. et al., Angiogenesis inhibitor TNP-470 inhibits murine cutaneous wound healing, <i>J. Surg. Res.</i> , 82 :268-274 (1999).	
	C35	Whalen, C.T. et al., Assay of TNP-470 and its two major metabolites in human plasma by high-performance liquid chromatography-mass spectrometry, <i>J. Chromatographic Sci.</i> , 40 :214-218 (2002).	
	C36	Brocchini, S. et al., Polymer-Drug conjugates: drug release from pendent linkers. in <i>Encyclopaedia of controlled release</i> (ed. Mathiovitz, E.) 786-816 (New York: Wiley, 1999).	
	C37	Duncan, R. et al., Polymer-drug conjugates, PDEPT and PELT: basic principles for design and transfer from the laboratory to clinic, <i>J. Controlled Release</i> , 74 :135-146 (2001).	
	C38	Vasey, P.A. et al., Phase I clinical and pharmacokinetic study of PK1 [N-(2-hydroxypropyl)methacrylamide copolymer doxorubicin]: first member of a new class of chemotherapeutic agents-drug-polymer conjugates, Cancer Research Campaign Phase I/II Committee, <i>Clinical Cancer Res.</i> , 5 :83-94 (1999).	
	C39	Seymour, L.W. et al., Tumour tropism and anti-cancer efficacy of polymer-based doxorubicin prodrugs in the treatment of subcutaneous murine B16F10 melanoma, <i>Br. J. Cancer</i> , 70 :636-641 (1994).	
	C40	Dvorak, H.F. et al., Identification and characterization of the blood vessels of solid tumors that are leaky to circulating macromolecules. <i>Am. J. Pathology</i> , 133 :95-109 (1988).	
	C41	Griffith, E.C. et al., Methionine aminopeptidase (type 2) is the common target for angiogenesis inhibitors AGM-1470 and ovalicin, <i>Chem. and Biol.</i> , 4 , 461-471 (1997).	
	C42	Auerbach, R. et al., Angiogenesis assays: problems and pitfalls, <i>Cancer Metastasis Rev.</i> , 19 :167-172 (2000).	
	C43	Seymour, L.W. et al., Hepatic drug targeting: phase I evaluation of polymer-bound doxorubicin., <i>J. Clinical Oncol.</i> , 20 :1668-1676 (2002).	

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Sheet	6	of	6	Attorney Docket Number	701039-52584-CIP

C44	Francis, G.E. et al., PEG-modified proteins. in <i>Stability of Proteins Pharmaceuticals (Part B)</i> (ed. Ahem TJ, M.M.) 235-263 (Plenum Press, New York, 1992).
C45	Ho, D.H. et al., Clinical pharmacology of polyethylene glycol-L-asparaginase, <i>Drug Metabolism Disposition</i> , 14:349-352 (1986).
C46	O'Reilly, M.S. et al., Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma, <i>Cell</i> , 79:315-328 (1994).
C47	Folkman, J. et al., Long-term culture of capillary endothelial cells, <i>Proc. Natl. Acad. Sci. USA</i> , 76:5217-5221 (1979).
C48	Waynforth, H.B. Routes and methods of administration, Intracerebral injection. in <i>Experimental and Surgical technique in the rat</i> , Vol. 2.9 34-36 (Academic Press, London, 1980).
C49	Bhargava, P. et al., A Phase I and pharmacokinetic study of TNP-470 administered weekly to patients with advanced cancer, <i>Clinical Cancer Res.</i> , 5:1989-1995 (1999).
C50	Seymour, L.W. et al., The pharmacokinetics of polymer-bound adriamycin, <i>Biochemical Pharmacology</i> , 39:1125-1131 (1990).
C51	Yeh, J.R. et al., The antiangiogenic agent TNP-470 requires p53 and p21 ^{CIP/WAF} for endothelial cell growth arrest, <i>Proc. Natl. Acad. Sci. USA</i> , 97:12782-12787 (2000).
C52	Zhang, Y. et al., Cell cycle inhibition by the anti-angiogenic agent TNP-470 is mediated by p53 and p21 ^{WAF1/CIP1} , <i>Proc. Natl. Acad. Sci. USA</i> , 97:6427-6432 (2000).
C53	Seymour, L.W. et al., N-(2-hydroxypropyl) methacrylamide copolymers targeted to the hepatocyte galactose-receptor: pharmacokinetics in DBA ₂ mice, <i>Br. J. Cancer</i> , 63:859-866 (1991).
C54	Folkman, J. Tumor angiogenesis. in <i>Accomplishments in cancer research</i> (eds. Wells, S.J. & Sharp, P.) 32-44 (Lippincott Williams & Wilkins, New York, 1998)

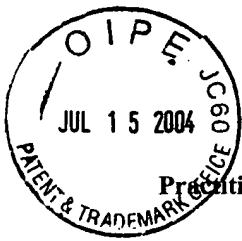
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Ronit Satchi-Fainaro; Judah M. Folkman
Application No.: 10/783,986 (CIP of PCT/US03/10976) Group No.: 1614
Filed: February 19, 2004 Examiner: To be assigned
For: TNP-470 SPECIES, POLYMER CONJUGATES AND USE THEREOF

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